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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,670	JACOBSEN ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-31* is/are pending in the application.

4a) Of the above claim(s) *22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 23-28* is/are rejected.

7)☒ Claim(s) *29-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on July 25, 2005.

Status of the Claims

2. Claims 21-54 were pending in the present application. Applicants canceled claims 32-54. Therefore, claims 21-31 are currently pending.

3. Applicant's response to the Restriction and/or Election of Species requirements is acknowledged (Applicant elected ***without traverse*** Group I, claims 21-31, see ***Response to Restriction and/or Election of Species*** below).

4. Please note: Applicant's elected species (compound shown on bottom of page 2 of 7/25/05 Response) was searched and was not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art. See MPEP § 803.02:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species***. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Claim 22 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species (see below i.e., ***Response to Restriction and/or Election of Species***). Applicants state, "Claims 21-31 read on the elected species" (e.g., see 7/25/05 Response, page 2). However, this statement appears to be in error as Applicants elected an "amino acid" $Liniker_1$ (e.g., see 7/25/05 Response, page 2, Subgroup 1 and compound at bottom of page), which is not encompassed by the Markush group of claim 22 (e.g., see claim 22, "$Liner_1$ and $Linker_2$ are independently selected from the set comprising diamines, diols, amino alcohols, and diacids [i.e., amino acid is not on the list]"). Therefore, claim 22 does not read on the elected invention.

6. Therefore, claims 21 and 23-31 are examined on the merits in this action.

Response to Restriction and/or Election of Species

7. Applicants' election of Group I (i.e., claims 21-31) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

8. Applicant's election of species is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

9. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

10. The information disclosure statement filed August 11, 2004, fails, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because two publications cited therein, marked N and R, lack page numbers, a necessary element for consideration. While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, these three publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPE § 609 C(1).

11. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action (e.g., 8/11/04).

Specification

12. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Objections to the Claims

13. Claims 29-31 are objected to because of the following informalities:

Claims 29-31 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim depends upon another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 29-31 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 21 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The present claims are directed to a broad library of "potential catalysts" having the following structure [solid support]-[linker$_1$]-[amino acid]-[linker$_2$]-[catalytic moiety] wherein Linker$_1$ and Linker$_2$ are independently selected from the group consisting of difunctional molecules with or without sidechains and/or stereocenters, the amino acid could be a natural or unnatural amino acid, and the catalytic moiety is selected from the set comprising the catalytically-active portions of known catalysts.

In contrast, Applicants' specification only discloses a library of "Strecker synthesis" catalysts with the "core" structure depicted on page 43 of the specification. In addition, Applicants only provide examples that contain phenyl groups for the "B" ring, a 1,2-disubstituted cycloalkyl for the "A" ring (if it exists), and an NH-Y-NH moiety for the linking group (e.g., see specification, page 43, bottom formula) wherein all he catalysts contain three essential metal binding ligands (i.e., an amino nitrogen atom (N) on the A ring, an immine nitrogen atom (N) on the A ring and a phenolic oxygen atom (O) on the B ring (e.g., see specification, page 42, paragraph 1, outlining the importance of a "tridentate Schiff base" i.e., the (N), (N), (O) metal ligands mentioned above).

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978); see also see also *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (CAFC 1991)). The "written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams formulas, etc., that fully set forth the claimed invention" (e.g., see *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966). In the present case, Applicants' specification only provides examples of Strecker synthesis catalysts (see above). In addition, when there is *substantial variation within the genus*, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, the variation within the genus would be enormous because Applicants do not limit the structure of the catalytic moiety in any way. In addition, the $Linker_1$, $Linker_2$ and catalytic moiety portions of the potential

catalysts can be independently selected to read on virtually an infinite number of structurally unrelated possibilities. For example, Hoveyda et al. state that a broad class of catalysts reacting with many different substrates cannot "by nature" be related (e.g., see Hoveyda, A. H. in "Handbook of Combinatorial Chemistry" Eds. Nicolaou, K. C.; Hanko, R.; Hartwig, W. Weinheim Germany: Wiley-VCH 2002, Vol. 2, page 991, "... chiral catalysts are often not general [catalysts]. Once we do come across an attractive catalyst, it is seldom effective for a wide range of substrates. This result is not surprising; a selective catalyst that recognizes a certain structural type with great fidelity cannot – by nature – recognize and associate with a gammut of substrates and promote reactions selectively") (8/11/04 IDS Reference LL). Thus, there is no structure/function relationship and/or identifying physiochemical properties that would otherwise allow Applicants to show possession of this broad genus. Furthermore, there is no known general method of synthesis for this broad class of compound.

The CAFC has also stated that a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)). Here, Applicants have failed to provide a definition, structure, formula or chemical name for any potential catalysts that fall outside the scope of the disclosed Strecker synthesis catalysts. In addition, the CAFC has stated that a genus, which is set forth only in functional terms, "... is not an adequate written description of

the genus because it does not distinguish the claimed genus from others, except by function" (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (1997)). Here, Applicants claim "catalytic moieties" that can only be distinguished from other compounds by their function (i.e., their ability to act as a catalyst), which was held to be impermissible in *Lilly*. Just as the generic term "cDNA" did not provide an adequate written description for the broad class of mammalian or vertebrate insulin DNA in *Lilly*, neither does the generic term "catalytic moiety" provide an adequate written description for the broad class of claimed compounds because the term "catalytic moiety" only defines by what it does (i.e., it ability to catalyze a reaction) rather than what it is (e.g., a chemical formula). Furthermore, stating that the catalytic moiety is "selected from the set comprising the catalytically-active portions of known catalysts" does not remedy these deficiencies because the catalytic portion of many "known" catalyst is unknown (e.g., see Newsam, J. M.; Schuth, F. "Combinatorial Approaches as a Component of High-throughput Experimentation (HTE) in Catalysis Research" *Comb. Chem. Biotechnol. Bioeng.* **1999**, *611*, 203-216, especially page 210, column 2, paragraphs 2-3, "Applications of HTE [High Throughput Experimentation] and combinatorial methods to heterogeneous catalysts are substantially different from those used in homogeneous catalysis ... First, we have little basis yet for formal library design, atomic-level active-site structure usually being, at best, poorly characterized. Second, detailed catalysts characterization is difficult. The averaged picture provided by X-ray and neutron scattering or EXAFS usually masks the active-site signatures, and local probes are likely to miss these critical, yet dilute fine details. Third, the optimal

performance of a catalysts is a balance between reactor configuration, reaction conditions, and the details of the catalyst itself; a change in one of the three elements requires concomitant adjustment in the two others. Fourth, scale-up of catalyst preparation even from the laboratory scale can be difficult. Firth, many catalysts only attain their desirable properties after time on stream, catalyst formation and deactivation processes being important in determining performance. Finally, the reaction conditions required for practical testing typically entail elevated temperatures and pressures, and various gas or liquid streams that might be flammable or toxic. Unsurprisingly, therefore, the field of accelerated combinatorial heterogeneous catalysis is still at an early stage of development"). In addition, the $Linker_2$ portion of Applicants' claimed catalyst also participates in catalysis (e.g., Applicants' elected N,N,O tri-dentate Strecker synthesis catalyst contains the 1,2-diamino-cyclhexane "diamine" linking group, which donates both nitrogens to the essential N,N,O group and thus would also participate as a catalytic moiety or, in the alternative, form part of the catalytic moiety). The prior art does not describe (i.e., via structure/function relationships and/or other distinguishing attributes) which "linkers" would be likely to perform such a function.

Thus, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention especially with regard to catalyst that fall outside the disclosed Strecker synthesis catalysts. It is well settled that claiming only a result (e.g., ability to act as a potential catalyst) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually

discovered or contemplated by the inventor, so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

16. Claims 21 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a library of catalysts that are used in the Strecker synthesis and possess the formula noted on page 43 of the specification, wherein the "B" ring is a phenyl, the "A" ring (if it exists) is a 1,2-disubstituted cycloalkyl, and the linking group is a NH-(C=X)-NH moiety choices, does not reasonably provide enablement for ***all*** "potential" catalysts used in ***any*** catalytic reaction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is an enablement rejection.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1 and 2) Breadth of the claims and nature of the invention: The breadth of the claims is enormous. Applicant's formula in claim 21 reads on an infinite number of compounds because several of the variable groups can contain an infinite number of possibilities that can all be independently changed to create the members of the library. For example, a variable number of amino acids, β-amino acids, γ-amino acids, non-natural amino acids, D and L amino acids and various spacer groups i.e. $Linker_1$ and $Linker_2$ containing various R side chains can be independently varied. In addition, the "catalytic moiety" bound to $Linker_2$ could encompass literally any structure.

Furthermore, it is not even possible to determine all of the compounds that would fall within the scope of a "potential catalyst." For example, catalytic activity (i.e., the functional language used to limit the claimed library members) is well recognized as being structure sensitive and not highly predictable See *Corona Co. v. Dovan*, 276 US 358 (U.S. 1928); also *In re Doumani*, 126 USPQ 408 (CCPA 1960). In addition, the term "potential catalyst" is not clearly defined further adding to the breadth of the claims and the unpredictable nature of the invention (see 35 USC 112, second paragraph, rejections below). Therefore, the Examiner contends that the breadth of the claims is enormous and the nature of the invention is unpredictable.

(3 and 5) The state of the prior art and the level of predictability in the art: Although libraries of solid-phase catalysts were known in the art at the time of filing,

only a limited number of such libraries were known (e.g., see rejections below) and the art is inherently unpredictable. Hoveyda states, "The discovery and identification of an effective chiral catalyst that promotes a chemical reaction with desirable levels of efficiency and selectivity is a difficult business. Because only small energy gaps separate an inactive or nonselective catalyst from one that is potent and selective (~1-2 kcal mol variance in transition-state energy), variations in reactivity and selectivity often arise unpredictably. Seemingly insignificant variations in the catalyst or substrate structure and reaction conditions (solvent polarity, temperature, etc.) can lead to entirely unexpected swings in yield, ee (enantiomeric excess), or both." (see Hoveyda, A. H. in "Handbook of Combinatorial Chemistry" Eds. Nicolaou, K. C.; Hanko, R.; Hartwig, W. Weinheim Germany: Wiley-VCH 2002, Vol. 2, page 991). Furthermore, this "unpredictability" is also well established in the law wherein catalytic activity (i.e., the functional language used to limit the claimed library members) is recognized as being structure sensitive and not highly predictable See *Corona Co. v. Dovan*, 276 US 358 (U.S. 1928); also *In re Doumani*, 126 USPQ 408 (CCPA 1960).

Furthermore, selecting "catalytically-active portions of known catalysts" from catalysts that are known to be reactive in solution would also lead to unpredictable results when coupled to a solid-support. For example, Shimizu et al states, "Reactions with immobilized ligands can be problematic for a number of reasons: Various solid supports contain Linker units with Lewis basic sites that may interact with transition metals. Moreover, on the solid support the aggregation state of the ligand-metal complexes, and thus the reactivity and selectivity patterns they generate, may significantly deviate from

those in solution. A literature survey revealed numerous examples of transformations with differing selectivity when performed on solid rather than in solution phases. Therefore, it was generally unclear whether data obtained from solid-phase studies could be reliably correlated with those in solution." (e.g., see Shimizu, K. D.; Cole, B. M.; Krueger, C. A.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. "Search for Chiral Catalysts Through Ligand Diversity: Substrate-Specific Catalysts and Ligand Screening on Solid Phase" *Angew Chem. Int. Ed.* September 1, 1997, *36(16)*, 1704-1707, especially pages 1704-05) (8/11/04 IDS, Ref. QQ).

(4) The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level

(6-7) The amount of direction provided by the inventor and the existence of working examples: The only embodiments of this invention that were actually prepared were based upon compounds that fall within the formula presented on page 43 of the specification, wherein the "B" ring is a phenyl, the "A" ring (if it exists) is a cycloalkyl, and the "J" linking group is a NH-(C=X)-NH moiety, which is clearly not representative of the broad scope that is currently claimed.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification for all the reasons asserted above does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the full scope of the claimed compounds. The number of examples provided in the disclosure does not reasonably correlate with the scope of the claims. Note that there must be sufficient

disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation. Please note that this is a "scope of enablement" rejection, which indicates that a portion of applicant's invention is indeed enabled by the specification, but points out that a much larger portion of the claimed invention is not enabled. Accordingly, in this respect an enablement rejection for scope is not internally or legally inconsistent with a finding that enabled embodiments are indeed either anticipated or rendered obvious by the prior art (e.g., see art rejections below).

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 21 and 23-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For ***claims 21, 23, 27 and 28***, the phrase "library of potential catalysts, and the individual members thereof" is vague and indefinite. For example, it is not clear how the

phrase "and the individual members thereof" further defines the claimed library as said claimed library already contains the individual members. Therefore, claims 21, 23, 27, 28 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. For ***claims 21 and 24-27***, the term "potential catalyst" is vague and indefinite. Does applicant mean to include only "potential" catalysts at the exclusion of "actual" catalysts or would an actual catalyst be a potential catalyst too? Conceivably, given an infinite number of chemical transformations, any molecule could be transformed into a catalyst? Thus, it is unclear how the term "potential catalyst" further defines the claimed compounds? If less than an infinite number of chemical transformations can be used to covert the potential catalyst to the active member, then it is unclear how many steps can be used i.e., the term "potential catalyst" (in this respect) is a relative term, which renders the claim indefinite and/or unclear. Therefore, claims 21, 24-27 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

C. For ***claims 21***, the term "difunctional molecules" in is vague and indefinite. For example, it is not clear whether there are only two functional groups in the molecule (i.e., to connect both sides to the resin and the catalytic moiety) or more than two when the additional "sidechains" (e.g., carboxylic acid, amino, etc.) are considered (i.e., does the term "difunctional" only refer to the backbone or to the backbone + sidechains). In addition, Applicant's elected 1,2-diamino-cyclohexane (i.e., $Linker_2$), which presumably constitutes a diamine (as disclosed in claim 22), would not be a "separate entity" (as disclosed in the generic formula of claim 21, separate from the amino acid and catalytic moiety) because the catalytic moiety (i.e., Applicants' elected Schiff base, see 7/25/05

Response, page 2, Subgroup 3) and the $Linker_2$ "share" the nitrogen atom (i.e., the nitrogen atom in the Schiff base). Applicants are requested to clarify and/or correct. Therefore, claims 21 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

D. For ***claim 21***, the phrase "with or without sidechains and/or stereocenters" in claims 21 is vague and indefinite. For example, it is not clear how the phrase "with or without" further limits the difunctional molecules. It would appear that the limitation "with or without" would include all possibilities. Applicants are requested to clarify and/or correct. Therefore, claims 21 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

E. For ***claim 21***, recites the limitation "the set" in the second to last line. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 21 and all dependent claims are rejected under 35 USC 112, second paragraph. The Examiner recommends the use of "a" set.

F. For ***claim 21***, recites the limitation "the catalytically active portions" in the second to last line. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 21 and all dependent claims are rejected under 35 USC 112, second paragraph. The Examiner recommends "one or more" catalytically active portions.

G. For ***claim 23***, the phrase "wherein the catalytic moiety is mono, di, tri, or tetradentate with respect to a substrate" is vague and indefinite. For example, metal chelates are generally classified by the number of bonds they make with a metal ion (e.g., 2 bonds = bidentate, 3 bonds, = tridentate, etc.). Here, it is not clear how a metal chelate

(i.e., the catalytic moiety) can be classified with respect to a substrate instead of a metal? Does Applicant intend the metal to be the substrate? If so, how is the metal ion transformed? Applicants are requested to clarify and/or correct. Therefore, claim 23 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 21 and 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Cole et al. (Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. "Discovery of Chiral Catalysts through Ligand Diversity: Ti-Catalyzed Enantioselective Addition of TMSCN to *meso* Epoxides" *Angew Chem. Int. Ed.* **1996**, *35(15)*, 1668-1671) (8/11/04 IDS Reference KK).

For ***claims 21 and 27-28***, Cole et al. disclose a library of solid-support linked tripeptide Schiff base catalysts for the Ti-catalyzed addition of trimethylsilycyanide to epoxides (e.g., pages 1668-1669, especially page 1669, first column, first paragraph; see also Experimental), which anticipates the claimed invention. For example, Cole et al. disclose catalysts that fall within the scope of Applicants' claims when the solid support sphere = PAC, the $Linker_1$ = glycine, the amino acid = {Tyr, Trp, Ser, Pro, Phe, Leu, Ile, Hyp, Gln, Thr, D-Thr, Chg, Cha, or Asn}, the $Linker_2$ = {Val, Leu, Thr, Ile, Gln, Ghg,

Cha, Asp, or Asn} and the catalytic moiety = 2-hydroxynapthalene or any of the other "aldehydes" shown in figure 1 (e.g., see Cole et al., page 1669-70, scheme 2 and Figure 1), which anticipates claim 21. Note that although testing was primarily carried out in solution, it was also done on the solid-support (e.g., see Cole et al., page 1670, left column, first paragraph, "Thus, enantioselective processes are possible with immobilized ligands"). Furthermore, Cole et al. disclose the use of a selected catalyst as a "lead structure" to identify improved members including reiterating the process between one and ten additional times (e.g., see page 1670, column 1, last paragraph, "To determine the best candidate for the amino acid unit AA1, ten ligand systems were prepared on solid support ... screened in a parallel fashion ... tLeu emerged as a superior AA1 unit. With tLeu as AA1 [i.e., a lead compound] and 2-hydroxyl-anapthaldehyde ... as the Schiff base, the search for the most appropriate AA2 unit ... led us to Thr(tBu) [i.e., process repeated a first time] ... With tLeu as AA1 and Thr(tBu) as AA2 [i.e., a second lead compound], thirteen aldehydes with a range of steric an electronic properties were ... screened [i.e., process repeated a second time]"). Alternatively, the Examiner argues that the limitations in claims 27 and 28 represent mere "intended use" language and, as a result, are not be afforded any patentable weight. If the prior art structure is capable of performing the intended use, then it meets the claim. The Office does not have the facilities to make a comparison and the burden is on the applicants to establish any difference between the transducing elements of the art and the instant claims. Se In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

For ***claims 23***, Cole et al. disclose the addition of TMSCN to cyclohexeneoxide in the presence of a Schiff-base metal catalyst (e.g., see Cole et al., page 1669, reaction (a), compounds 1 and 2). Since the only possible ligand that could bind to the metal catalyst is the epoxide oxygen (i.e., the rest of the molecule is unreactive hydrocarbon) and since oxygen is a good ligand for the hard metals that are used in the reaction, the Examiner maintains that this reaction represents a situation wherein the catalytic moiety is monodentate with respect to the ligand (i.e., more than one ligand would be sterically hindered by the bulky cyclohexyl group). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Alternatively, the Examiner argues that the phenolic oxygen, imine nitrogen and adjacent carbonyl oxygen form a "tridentate" metal ligand in similar fashion to the Strecker synthesis catalyst disclosed by Applicant (e.g., see 35 U.S.C. 112, second paragraph rejection above).

For **claims 24-26**, Cole et al. disclose a library of 32,000 members (40×40×20) different chiral catalysts could be made from the (20 natural L amino acids + 20 natural D amino acids) × (20 natural L amino acids + 20 natural D amino acids) × 20 different aldehydes that were used to produce the imines, which reads on claims 24-26 because 32,000 is greater than 100 (claim 24), 1,000 (claim 25), and 10,000 (claim 26).

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 21 and 23-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of .S. Patent No. 6,709,824 B2 (referred to herein as '824) in view of Sparrow (Sparrow, J. T. "An Improved Polystyrene Support for Solid Phase Peptide Synthesis" *J. Org. Chem.* **1976**, *42(8)*, 1350-1353). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examiner application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, claims 1-6 of '824 patent recite a Schiff base-containing library that reads on Applicants' claimed "potential" catalysts. For example, '824 patent discloses N=C-Ar (with HX, R_3 and OR_4 substitutions) as the Schiff base (e.g., see '824, claim 3), which falls entirely within

the scope of Applicants' claimed Schiff base-containing catalytic moiety. The '824 patent also discloses Applicants' elected 1,2-diamino-cyclohexane "diamine" linker and variations thereof (e.g., see '824, claim 3, when n=1 and R_2 = H), which falls entirely within the scope of Applicants' claimed difunctional linkers. The '824 patent also discloses an "amino acid" portion when X represents O (e.g., see claim 3, "X represents ... O, S, or NR"). A generic chemical formula will anticipate (or render obvious) a species covered by the formula when the species can be "at once envisaged" from the formula (e.g., see MPEP § 2131; see also *In re Petering* 133 USPQ 275 (CCPA 1962)). Here, there are only three possibilities for X, which would render the amino acid version (i.e., X = O) immediately envisioned. The '824 patent also discloses "R" as a solid-support, which is defined in the specification to include resins like polystyrene (e.g., see claim 1, element R109; see also column 14, lines 40-46, "The term 'polymeric support', as used herein, refers to ... polystyrene resins"; see also MPEP § 804, "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). The '824 patent also teaches the use of mono-, di-, tri, or tetra-dentate catalytic moieties (e.g., see claim 1 wherein the tri-dentate N, N, O catalytic moiety is disclosed; see also 35 U.S.C. 112, second paragraph rejection above). The '824 patent also recites a library comprising at least ten thousand compounds (e.g., compare claims 24-24 of the present application to claims 4-6 of '824). The '824 patent does not state that the catalyst library was "used" as a lead structure as in the present application (e.g., see present application, claims 27 and 28). However, the Examiner contends that this represents merely "intended use" language that is not afforded any patentable weight because it does not lead to a structural difference. If the prior art structure is capable of performing the intended use, then it meets the

claim. The Office does not have the facilities to make a comparison and the burden is on the applicants to establish any difference between the transducing elements of the art and the instant claims. Se In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The only difference is that the '824 patent fails to claim a difunctional $Linker_1$. The '824 patent only discloses a direct attachment of the amino acid to the polymer. However, Sparrow teaches the use of linkers such as the difunctional "amino acid" linker Boc-11-aminohendecanoic to make such an attachment (e.g., see Scheme I; see also Experimental Section), which falls within the scope of Applicants' claimed difunctional $Linker_1$.

It would have been *prima facie* obvious to use the amino acid linker as disclosed by Sparrow for use in solid-phase synthesis reactions employing a polystyrene support as disclosed by the '824 patent (e.g., see claim 1, element R109; see also column 14, lines 40-46, "The term 'polymeric support', as used herein, refers to ... polystyrene resins") because Sparrow explicitly states that such linkers should be used for this purpose (e.g., see Sparrow, abstract, "By placing a long spacer chain between the point of attachment of the first amino acid and the polystyrene support, an improved resin was obtained"). One having ordinary skill in the art would have been motivated to make such a modification because Sparrow explicitly states that higher yields and/or increased purity can be obtained by using the linker (e.g., see Sparrow, abstract; see also Results and Discussion). Finally, a person of skill would have reasonably expected to be successful because Sparrow clearly shows that such a linker can be coupled to an amino acid, which is exactly what is required by the '824 patent.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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